UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/809,965	03/25/2004	Dave S.B. Hoon	89212.0016	7891

7590 03/06/2008

HOGAN & HARTSON, L.L.P.
1999 Avenue of the Stars
Suite 1400
Los Angeles, CA 90067

EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	
MAIL DATE	DELIVERY MODE
03/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/809,965	HOON ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 November 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,5,7-13,15-18 and 20-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,5,7-13,15-18 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Applicants' response to the office action field on November 29, 2007 has been considered and acknowledged.

Status of the application

2. Currently claims 1-2, 4-5, 7-13, 15-18, 20-25 are pending. Claims 3, 6, 14, 19, and 26-31 are cancelled. Claims 1, 7, 13, 15-18 are amended. Applicants' arguments and the amendment have been fully considered and deemed persuasive in-part for the reasons that follow.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

A. Claims 1, 5, 7-13, 17-18, 20-25 rejected under 35 U.S.C. 102(a) as being anticipated by Lecomte et al. (Int. J. Cancer, Vol. 100, pp. 542-548, 2002).

Lecomte et al. teach a method of claim 1, 7-13, 17-18, 20-25, detecting DNA markers in colorectal cancer comprising:

providing a cell-free bone marrow sample from a subject (see page 542, col. 1, abstract, page 543, co. 1, paragraph 1 under materials and methods section);

detecting one or more DNA markers in the sample, wherein the DNA markers are indicative of LOH or hypermethylation or DNA markers (KRAS) or a combination of LOH and hypermethylation (see page 543, col. 1, paragraph 2-5, col. 2, paragraphs 1-4).

With regard to claim 7, Lecomte et al. teach that said DNA markers include KRAS mutation detection (see page 543, col. 1, paragraph 5).

With regard to claims 13, 17-18, 22, 25, Lecomte et al. teach that said sample is a plasma sample (see page 543, col. 1, paragraph 4 under materials and methods section).

With regard to claims 17-18, 20, 23, Lecomte et al. teach detecting a combination of LOH and hypermethylation of markers indicative of cancer (see page 542, col. 1 abstract, page 543, col. 1, paragraph 5 under materials and methods section, page 544, col. 1, paragraph 1 under Results).

With regard to claim 5, Lecomte et al. teach that said hypermethylation DNA marker comprises p16 (see page 542, col. 1 abstract, page 543, col. 1, paragraph 5 under materials and methods section, page 544, col. 1, paragraph 1 under Results).

With regard to claims 8, 10, 12, 21, 23, Lecomte et al. teach that the cancer is colorectal cancer (see page 542, col. 1 abstract, page 543, col. 1, paragraph 5 under materials and methods section, page 544, col. 1, paragraph 1 under Results).

With regard to claims 22, 25, Lecomte et al. teach that the sample is from plasma and tissue samples (see page 543, col. 1, paragraph 1-4). Accordingly Lecomte et al. anticipates the instant claims.

B. Claims 1-2, 5, 7, 9, 11, 13, 17-18, 20, 22-23, 25 rejected under 35 U.S.C. 102(a) as being anticipated by Bearzatto et al. (Clin Cancer Res., Vol. 8, pp. 3782-3787, December 2002).

Bearzatto et al. teach a method of claim 1, 7, 9, 11, 13, 17, 18, 20, 22- 23, 25, detecting DNA markers in a sample comprising:

providing a cell-free bone marrow sample from a subject (see page 3783, col. 1, paragraph 2 under materials and methods section);

detecting one or more DNA markers in the sample, wherein the DNA markers are indicative of LOH or hypermethylation or DNA markers (K-ras) or a combination of LOH and hypermethylation (see page 3783, col. 2, paragraph 1-3, page 3784, col. 1, paragraphs 1-4, page 8785, col. 2, paragraph 3, page 3786, table 2, col. 1, paragraph 1under discussion section).

With regard to claim 7, Bearzatto et al. teach that said DNA markers include KRAS mutation detection (see page 3784, col. 1, paragraph 2-3).

With regard to claims 1, 7, 9, 11, 13, 17-18, 22, 25, Bearzatto et al. teach that said sample is a plasma sample (see page 3783, col. 1, paragraph 2 under materials and methods section).

With regard to claims 17-18, 20, 23, Bearzatto et al. teach detecting a combination of LOH and hypermethylation of markers indicative of cancer (see page 3782, col. 1 abstract, page 3786, col. 1, paragraph 1 under discussion section, page 3787, col. 1, paragraph 1).

With regard to claim 2, Bearzatto et al. teach that the DNA markers are on 3p region (see page 3783, col. 2, paragraph 4).

With regard to claim 5, Bearzatto et al. teach that said hypermethylation DNA marker comprises p16 (see page 3783, col. 2, paragraph 1). Accordingly Bearzatto et al. anticipates the instant claims.

C. Claims 1, 5, 7, 9, 11, 13, 17-18, 20, 22-23, 25 rejected under 35 U.S.C. 102(a) as being anticipated by Dominguez et al. (Clin Cancer Res., Vol. 8, pp. 980-985, April 2002).

Dominguez et al. teach a method of claim 1, 7, 9, 11, 13, 17, 18, 20, 22- 23, 25, detecting DNA markers in a sample comprising:

providing a cell-free bone marrow sample from a subject (see page 980, col. 2, paragraph 1 under materials and methods section);

detecting one or more DNA markers in the sample, wherein the DNA markers are indicative of LOH or hypermethylation or DNA markers (K-ras, p53) or a combination of LOH and hypermethylation (see page 980, col. 1, abstract, page 981, col. 1, paragraph 2, col. 2, paragraph 1-3, page 982, Fig. 1).

With regard to claim 7, Dominguez et al. teach that said DNA markers include KRAS mutation detection (see page 981, col. 2, paragraph 2, page 982, Fig. 1, col. 1, paragraph 3 under results section).

With regard to claims 1, 7, 9, 11,13, 17-18, 22, 25, Dominguez et al. teach that said sample is a plasma sample (see page 980, col. 2, paragraph 1 under materials and methods section, page 982, Fig. 1).

With regard to claims 17-18, 20, 23, Dominguez et al. teach detecting a combination of LOH and hypermethylation of markers indicative of cancer and stage of cancer and poor prognosis of cancer (see page 982, Fig. 1, col. 2, paragraph 1-2, page 980, col. 1 abstract).

With regard to claim 5, Dominguez et al. teach that said hypermethylation DNA marker comprises p16 (see page 981, col. 2, paragraph 3, page 982, Fig. 1). Accordingly Dominguez et al. anticipates the instant claims.

D. Claims 9-13, 15, 17-18, 20-25, rejected under 35 U.S.C. 102(a) as being anticipated by Silva et al. (Annals of Surgical Oncology, Vol. 9(1), pp. 71-76, 2002).

Silva et al. teach a method of claims 9-13, 15, 17-18, 20-25 detecting DNA markers in a sample comprising:

providing a cell-free bone marrow sample or a tissue sample from a subject (see page 72, col. 1, paragraph 1-2 under Patients and methods section);

detecting one or more DNA markers in the sample, wherein the DNA markers are indicative of LOH or hypermethylation or DNA markers or a combination of LOH and hypermethylation (see page 72, col. 2, paragraph 2, page 73, col. 1, paragraphs 1-2, col. 2, paragraph 2-3 under results section).

With regard to claim 15, Silva et al. teach that the DNA markers are selected from D17S855, D17S654, D16S421, D10S197, mutation in p53 gene and hypermethylation marker p16 (see page 71, abstract, page 72, col. 2, paragraph 2, page 73, col. 1, paragraph 1-2).

With regard to claims 9,11,13, 15, 17-18, 20, 22-23, 25, Silva et al. teach that said sample is a plasma sample or tissue sample (see page 72, col. 1, paragraph 1-2 under patients and methods section).

With regard to claims 13, 15, 17-18, 20, 23, Silva et al. teach detecting a combination of LOH and hypermethylation of markers indicative of cancer (see page 71, abstract, page 74, , col. 1, paragraph, table. 1).

With regard to claim 10, 12, 21, 24, Silva et al. teach that the cancer includes breast cancer (see page 71, abstract, page 72, col. 1, paragraph 1 under patients and methods section).

With regard to claims 22, 25, Silva et al. teach that said sample is from plasma and tumor tissue (see page 72, col. 1, paragraphs 1-2 under patients and methods section). Accordingly Silva et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

A. Claims 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lecomte et al. (Int. J. Cancer, Vol. 100, pp. 542-548, 2002) in view of Silva et al. (Annals of Surgical Oncology, Vol. 9(1), pp. 71-76, 2002).

Locomte et al. teach a method of detecting DNA markers in cell-free bone marrow cells as discussed above in section 3A.

However Lecomte et al. did not teach DNA markers as claimed in claim 4.

Silva et al. teach a method of detecting DNA markers in plasma samples, wherein the DNA markers are selected from D17S855, D17S654, D16S421, D10S197, mutation in p53 gene and hypermethylation marker p16 (see page 71, abstract, page 72, col. 2, paragraph 2, page 73, col. 1, paragraph 1-2).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting DNA markers in cancer samples as taught by Locomte et al. with the DNA markers as taught by Silva et al. for the purpose of developing a sensitive method for detecting a cancer. An ordinary person skilled in the art would have a reasonable expectation of success that the combination of the method of Lecomte et al. and the DNA markers of Silva et al. would result in a sensitive method for detecting cancer because Silva et al. explicitly taught the use of microsatellite markers in detecting cancer and the association of said markers in the prognosis of cancer (see page 71, abstract) and such modification of the method is considered as obvious over the cited prior art.

B. Claims 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Silva et al. (Annals of Surgical Oncology, Vol. 9(1), pp. 71-76, 2002) in view of Kawakami et al (J Natl. Cancer Institute, Vol. 92, No. 22, 2000).

Silva et al. teach a method of detecting DNA markers in plasma samples, wherein the DNA markers are selected from D17S855, D17S654, D16S421, D10S197, mutation in p53 gene and hypermethylation marker p16 (see page 71, abstract, page 72, col. 2, paragraph 2, page 73, col. 1, paragraph 1-2).

Although Silva teach hypermethylation markers, Silva et al. did not specifically teach hypermethylation markers as APC, cyclin D2 promoter, RASSF1A, MGMT or GSTP1.

Kawakami et al. teach a method of detecting hypermethylated APC DNA in plasma, wherein Kawakami et al. teach that hypermethylated APC may be a useful biomarker in detecting biologically aggressive cancer (see page 1805, col. 1, Summary).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method for detecting DNA markers in cancer samples as taught by Silva et al. with the hypermethylated DNA markers as taught by Kawakami et al. for the purpose of developing a sensitive method for detecting a cancer. An ordinary person skilled in the art would have a reasonable expectation of success that the combination of the method of Silva et al. and the hypermethylated DNA markers of Kawakami et al. would result in a sensitive method for detecting cancer because Kawakami et al. teach that hypermethylated APC may be a useful biomarker in detecting biologically aggressive cancer (see page 1805, col. 1, Summary) and such modification of the method is considered as obvious over the cited prior art.

Response to arguments:

5. With regard to the objection to the specification, Applicants' arguments and the amendment along with the sequence listing have been fully considered and the objection is withdrawn herein in view of the amendment.

6. With regard to the rejection of claims 13-14, 17-25 under 35 USC 102(a) as being anticipated by Yang et al., Applicants' amendment and arguments were fully considered and found persuasive in-part. The rejection of claims 13-14, 17-18 is withdrawn herein in view of the amendment. However with regard to the claims 20-25, the rejection is maintained herein. Applicants argue that Yang et al. does not teach association of a combination of LOH and hypermethylation DNA markers with an advanced stage of cancer or poor prognosis of cancer and thus Yang et al. does not anticipate the claims. Applicants' arguments were found

unpersuasive because the method of claims 20 and 33 require only ' detecting a combination of LOH and hypermethylation DNA markers and its association to said limitations, since Yang et al. teach an association of said combination of DNA markers with cancer, Yang et al. teachings inherently teach said association of the markers with an advanced stage of cancer or poor prognosis of cancer. Further the claims as recited would not distinguish from the teachings of Yang et al. because the claims do not require detecting any difference or variation in the levels of said combination of DNA markers that is associated with an advanced stage or poor prognosis. Thus the instant claims as presented does encompass said limitations inherently and the claims as presented do not distinguish from the method of Yang et al., since the association is based on only a combination of said DNA markers with an advanced stage of cancer or poor prognosis of cancer.

7. With regard to the rejection of claims 13-15, 17, 19-20, 22-23, 25 under 35 USC 102(b) as being anticipated by Kondo et al., Applicants' amendment and arguments were fully considered and found persuasive in-part. The rejection of claims 13-15, 17-18 is withdrawn herein in view of the amendment. However, as discussed above, the same arguments would apply herein with regard to Kondo et al. reference. The instant claims 20, 22-23, 25 as presented do not distinguish from the method of Kondo et al. since the instant claims recite an association of a combination of LOH and hypermethylation DNA markers with an advanced stage of cancer or poor prognosis of cancer, thus Kondo et al. inherently teaches said association and the rejection is maintained herein for claims 20, 22-23, and 25.

8. With regard to the rejection of claims 1, 7-12 under 35 USC 102(b) as being anticipated by Hoon et al., Applicants' amendment and arguments were fully considered and found persuasive. The rejection is withdrawn herein in view of the amendment.

9. With regard to the rejection of claims 2-3, 5-6 under 35 USC 103(a) as being obvious over Hoon et al. in view of Anker et al., Applicants' amendment and arguments were fully considered and found persuasive. The rejection is withdrawn herein in view of the amendment.

10. With regard to the rejection of claims 4 under 35 USC 103(a) as being obvious over Hoon et al. in view of Fujiwara et al., Applicants' amendment and arguments were fully considered and found persuasive. The rejection is withdrawn herein in view of the amendment.

11. With regard to the rejection of claims 16 under 35 USC 103(a) as being obvious over Kondo et al. in view of Anker et al., Applicants' amendment and arguments were fully considered and found persuasive. The rejection is withdrawn herein in view of the amendment.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Suryaprabha Chunduru/

Primary Examiner, Art Unit 1637